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| 10/010,593 | 11/09/2001 | Hiroaki Yamamoto | 06501-052002 | 4357 |

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| EXAMINER | |
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| RAMIREZ, DELIA M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | |

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/010,593 | YAMAMOTO, HIROAKI | |
| | Examiner | Art Unit | |
| | Delia M. Ramirez | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *10-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. 09/478,163.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/9/01,1/28/02,5/*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Application*

Claims 10-20 are pending.

Applicant's preliminary amendment canceling claims 1-9 in a communication filed on 11/9/2001 is acknowledged.

Applicant's preliminary amendment of claims 10 and 12 in a communication filed on 2/20/2002 is acknowledged.

Applicant's preliminary amendment of claims 10 and 12, amendments to the specification, and addition of claims 13-20 in a communication filed on 2/25/2002 is acknowledged.

### *Specification*

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

***Priority***

2. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to JAPAN 11/002039 filed on 01/07/1999.

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. DIV of 09/478,163 filed on 01/05/2000.

***Information Disclosure Statement***

4. The information disclosure statements (IDS) submitted on 11/9/2001, 1/28/2002, and 5/14/2002 are acknowledged. Reference AL in the IDS filed on 1/28/2002 lacks a publication date, it is not in English, and lacks the country or patent office where it was filed. As such, it has not been considered. The remaining references in the IDSs filed are in compliance with the provisions of 37 CFR 1.97 and are being considered by the Examiner.

***Claim Objections***

5. Claim 10 is objected to due to the recitation of "electron acceptor for oxidoreductase expressed by said microorganism is enhanced by the method comprising culturing the microorganism...". For clarity and to avoid redundancy, it is suggested that the term be replaced with "electron acceptor for an oxidoreductase expressed by said microorganism is enhanced by culturing the microorganism...". Appropriate correction is required.

6. Claim 12 is objected to due to the recitation of "oxidize either (S)-enantiomer or (R)-enantiomer ....oxidoreductase expressed by said .....is enhanced by the method comprising culturing the microorganism...". For clarity and to avoid redundancy, it is suggested that the term be replaced with "oxidize either an (S)-enantiomer or (R)-enantiomer ....an oxidoreductase expressed by said .....is enhanced by culturing the microorganism...". Appropriate correction is required.

***Claim Rejections - 35 USC § 112, Second Paragraph***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 12-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 12 (claims 13-20 dependent thereon) is indefinite in the recitation of "a microorganism with racemic alcohol to specifically oxidize either (S)-enantiomer or (R)-enantiomer in the racemate.." as there is no antecedent basis for the term "racemate". For examination purposes, it will be assumed that the term refers to "racemic alcohol". Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 10-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 10 is directed to a method for producing an oxidized form of a genus of organic compounds, wherein the method comprises contacting the organic compounds with a microorganism whose activity to regenerate a genus of electron acceptors for a genus of oxidoreductases expressed in said microorganism is enhanced by culturing said microorganism at a dissolved oxygen concentration of 50% saturation or less. Claim 11 is directed to the method of claim 11 except that the method produces a

genus of alcohols. Claim 12 is directed to a method for producing a genus of optically active alcohols from racemic alcohol mixtures by using a microorganism capable of producing a genus of oxidoreductases, wherein said oxidoreductases specifically oxidize either the (S) or (R) enantiomer in the racemic alcohol mixtures, and wherein said microorganism is cultivated at a dissolved oxygen concentration of 50% or less saturation in order to regenerate a genus of electron acceptors for the oxidoreductases. Claims 13-14 are directed to the methods of claims 10 or 12 with added limitations regarding the % dissolved oxygen concentration in the culture. Claim 15 is directed to the methods of claims 10 or 12 with limitations regarding the identity of the electron acceptor. Claim 16 is directed to the methods of claims 10 or 12 wherein the oxidoreductase is alcohol dehydrogenase. Claim 17 is directed to the methods of claims 10 or 12 wherein the oxidoreductase is from C. parapsilosis. Claims 18-19 are directed to the methods of claims 10 or 12 with limitations regarding the identity of the microorganism. Claim 20 is directed to the methods of claims 10 or 20 wherein the microorganism is genetically engineered to produce the oxidoreductase.

While the specification discloses the culturing of E. coli JM109 [pKK-CPA-1], wherein pKK-CPA1 comprises a gene from C. parapsilosis encoding a secondary alcohol dehydrogenase, at low dissolved oxygen concentrations (Examples 4 and 5), and the increase in specific alcohol dehydrogenase activity at low dissolved oxygen concentrations (Table 1 and Table 2), the specification fails to provide any information regarding (1) the specificity of the alcohol dehydrogenase encoded in pKK-CPA1, (2) other alcohols which can be oxidized by the alcohol dehydrogenase encoded in pKK-CPA1, (3) other oxidoreductases from other organisms, the identity of those organic compounds which can be oxidized by these oxidoreductases, and their corresponding electron acceptors (4) other oxidoreductases from C. parapsilosis which can be used to oxidize any organic compound or to produce optically active alcohols, (5) the electron acceptors of the oxidoreductases of (4), and (6) other oxidoreductases from other organisms which specifically oxidize either the (S) or (R) enantiomer in racemic alcohol mixtures, the

identity of those alcohols which can be oxidized by these oxidoreductases, and their corresponding electron acceptors. The specification fails to describe other representative species of the genus of oxidoreductases, alcohol dehydrogenases, organic compounds, alcohols, electron acceptors, and C. parapsilosis oxidoreductases required to practice the claimed method. Furthermore, the specification fails to provide any structural feature common to all the members of the genera of compounds recited in the claims. Many functionally and structurally unrelated compounds are encompassed by these claims. The specification provides one oxidoreductase from C. parapsilosis, one organic compound, 1,3 butanediol, and 5 electron acceptors, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of the claimed method. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

12. Claims 10-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a method for oxidizing (S)-1,3-butanediol by contacting (S)-1,3-butanediol with a microorganism capable of expressing the C. parapsilosis alcohol dehydrogenase encoded in pKK-CPA1, wherein said microorganism is cultivated at low dissolved oxygen concentrations, and (2) a method for producing optically active (R)-1,3-butanediol by contacting a racemic alcohol mixture containing (S)-1,3-butanediol with a microorganism capable of expressing the C. parapsilosis alcohol dehydrogenase encoded in pKK-CPA1, wherein said microorganism is cultivated at low dissolved oxygen conditions, does not reasonably provide enablement for (1) a method for producing an oxidized form of any organic compound or alcohol, wherein the method comprises contacting the organic compound/alcohol with a microorganism whose activity to regenerate any electron acceptor for any oxidoreductase expressed in said microorganism is enhanced by culturing said microorganism at a low dissolved oxygen concentration, or (2) a method for producing any optically active alcohol from any racemic alcohol

mixture by using a microorganism capable of producing any oxidoreductase, any C. parapsilosis oxidoreductase, or any alcohol dehydrogenase, wherein said oxidoreductase/alcohol dehydrogenase specifically oxidizes either the (S) or (R) enantiomer in the racemic alcohol mixture, and wherein said microorganism is cultivated at a low dissolved oxygen concentration in order to regenerate any electron acceptor for said oxidoreductase/alcohol dehydrogenase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims, as described above, is not commensurate with the enablement provided in regard to the extremely large number of organic compounds, oxidoreductases, alcohol dehydrogenases, electron acceptors, alcohols, and C. parapsilosis oxidoreductases encompassed by the claimed method. As indicated above, the specification fails to provide any information as to (1) the specificity of the alcohol dehydrogenase encoded in pKK-CPA1, (2) other alcohols which can be oxidized by the alcohol dehydrogenase encoded in pKK-CPA1, (3) other oxidoreductases from other organisms, the identity of those organic compounds which can be oxidized by these oxidoreductases, and their corresponding electron acceptors (4) other oxidoreductases from C. parapsilosis which can be used to oxidize any organic compound or to produce optically active alcohols, and the corresponding electron acceptors for such oxidoreductases, and (5) other oxidoreductases from other organisms which specifically oxidize either the (S) or (R) enantiomer in racemic alcohol mixtures, the identity of those alcohols which can be oxidized by these oxidoreductases, and their corresponding electron acceptors. The specification

provides no structure for the oxidoreductases/alcohol dehydrogenases required for the claimed method nor does it provide any clue as to which are the critical structural elements in any polypeptide which would correlate with the desired activity/specificity. Furthermore, the specification is silent as to (1) how one of skill in the art would isolate the required enzymes, (2) the identifying characteristics in any protein which would provide one of skill in the art a reasonable indication as to the kind of organic compounds or alcohols which can be oxidized by the oxidoreductases/alcohol dehydrogenases required in the claimed method, (3) the identity of those organisms which can be used in the claimed method as not all microorganisms can be cultured under low oxygen conditions or anaerobic conditions, (4) the identity of those electron acceptors which can be regenerated under low aeration conditions, and (5) which are the structural characteristics in any C. parapsilosis protein which are associated with enantiomer-specific alcohol dehydrogenase activity.

Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the structural elements, specificities and electron acceptors of all the enzymes required, as well as the lack of knowledge as to the identity of the organic compounds/alcohols which can be oxidized by all the enzymes recited, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the full scope of the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

13. It is noted that if the claims are amended to limit the alcohol dehydrogenase to that of pKK-CPA1, a biological deposit made in accordance with 37 CFR 1.801-1.809 may be required to comply with the enablement requirements.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 10-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al., Biosci. Biotechnol. Biochem. 63:1051-1055, June 1999) in view of Matsushita et al. (J. Bacteriol. 177:6552-6559, 1995).

Yamamoto et al. teaches the cloning and expression in E. coli of a gene encoding for a Candida parapsilosis secondary alcohol dehydrogenase. The dehydrogenase of Yamamoto et al. is stereo specific for (S)-1,3-butanediol and oxidizes (S)-1,3-butanediol to 4-hydroxy-2-butanone (page 1055, Abstract, left column). E. coli JM109 was transformed with plasmid pKK-CPA1, which contains the C. parapsilosis gene encoding the dehydrogenase. Yamamoto et al. also teaches the production of (R)-1,3-butanediol and 4-hydroxy-2-butanone by contacting E. coli JM109 (pKK-CPA1) with a racemic alcohol mixture (page 1055, both columns; Figure 3). Yamamoto et al. indicates that the asymmetric oxidation using this E. coli strain did not require an additional NAD+ regeneration system and that chiral alcohols have so far been synthesized by the asymmetric reduction method, which requires an additional NADH or NADPH

regeneration system (page 1055, left column). Yamamoto et al. does not teach producing (R)-1,3-butanediol by culturing E. coli JM109 (pKK-CPA1) at a dissolved oxygen concentration of 50%, 20%, 10% or less saturation. Matsushita et al. teaches that alcohol dehydrogenase (ADH) activity from Acetobacter aceti and Gluconobacter suboxydans decreases under high aeration conditions and increases under low aeration conditions (Abstract; page 6558, left column, Discussion, lines 24-27). Matsushita et al. also discloses culturing these bacterial strains under low concentrations of dissolved oxygen (low aeration conditions) and obtaining an increase in the dehydrogenase activity (page 6555, left column, lines 2-6).

Claims 10 and 11 are directed in part to a method for producing an oxidized form of an alcohol, wherein the method comprises contacting the alcohol with a microorganism whose activity to regenerate an electron acceptor for an oxidoreductase expressed in said microorganism is enhanced by culturing said microorganism at a dissolved oxygen concentration of 50% saturation or less. Claims 12-20 are directed in part to a method for producing an optically active alcohol from a racemic alcohol mixture by using a microorganism capable of producing a Candida parapsilosis alcohol dehydrogenase, wherein said microorganism is cultivated at a dissolved oxygen concentration of 50%, 20%, 10% or less saturation in order to regenerate an electron acceptor for the alcohol dehydrogenase, and wherein said organism is E. coli.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the method, as taught by Yamamoto, by cultivating the cells at a dissolved oxygen concentration of 50%, 20%, 10% or less saturation. A person of ordinary skill in the art is motivated to practice the method of Yamamoto et al. at a concentration of dissolved oxygen of 50% , 20%, 10% or less saturation in view of the teachings of Matsushita et al. regarding the increase in alcohol dehydrogenase activity upon cultivation at low aeration conditions. One of ordinary skill in the art has a reasonable expectation of success at practicing the method of Yamamoto et al. at the recited dissolved oxygen

conditions since Matsushita et al. teaches that alcohol dehydrogenase activity can be increased by decreasing aeration in the culture. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

***Double Patenting***

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 10-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 40 of copending Application No. 10/147003. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claims 10 and 11 are directed in part to a method for producing an oxidized form of an alcohol, wherein the method comprises contacting the alcohol with a microorganism whose activity to regenerate an electron acceptor for an oxidoreductase expressed in said microorganism is enhanced by culturing said

microorganism at a dissolved oxygen concentration of 50% saturation or less. Claims 12-20 are directed in part to a method for producing an optically active alcohol from a racemic alcohol mixture by using a microorganism capable of producing a Candida parapsilosis oxidoreductase, wherein said microorganism is cultivated at a dissolved oxygen concentration of 50%, 20%, 10% saturation or less, in order to regenerate an electron acceptor for the oxidoreductase.

Claim 40 of copending Application No. 10/147003 is directed in part to a method for producing (R)-1,3-butanediol, wherein said method comprises producing (R)-1,3-butanediol and 4-hydroxy-2-butanone by oxidizing (S)-1,3-butanediol from a racemic 1,3-butanediol mixture with a microorganism which produces a Candida parapsilosis secondary alcohol dehydrogenase. According to the specification of copending Application No. 10/147003 (page 25, lines 1-13), a preferred embodiment of the invention is practicing the claimed method in combination with an enzyme reaction for regenerating NADH, wherein said regeneration can be obtained by maintaining a low dissolved oxygen concentration. The secondary alcohol dehydrogenase from Candida parapsilosis will oxidize (S)-1,3-butanediol (alcohol) into 4-hydroxy-2-butanone, therefore increasing the concentration of (R)-1,3-butanediol in the racemic alcohol mixture. (R)-1,3-butanediol is an optically active alcohol.

Claims 10-20 are deemed obvious over claim 40 of copending Application No. 10/147003 as it would have been obvious to one of skill in the art at the time the invention was made to practice the claimed method with limitations regarding the % dissolved oxygen concentration as recited in claims 10-20 of the instant application. One of skill in the art would have been motivated to practice the claimed invention at the recited dissolved oxygen concentrations in view of the preferred embodiment disclosed in copending Application No. 10/147003 regarding the low dissolved oxygen concentration required to obtain regeneration of NADH. One of ordinary skill in the art has a reasonable expectation of success at practicing the claimed method at the recited dissolved oxygen concentrations since all that is required is adjustment of the dissolved oxygen concentration during culturing of the microorganism. Therefore, the

invention of claims 10-20 would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

***Conclusion***

19. No claim is in condition for allowance.

20. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 15, 2004

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1600~~
1600